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**RAW SEQUENCE LISTING**
**PATENT APPLICATION** *US/08/485,943*

AU 1804

DATE: 04/17/96
TIME: 14:57:01

*INPUT SET: S9945.raw*

> This Raw Listing contains the General Information Section and those Sequences containing ERRORS.

Does Not Comply
SEQUENCE LISTING Corrected Diskette Needed

*See remarks throughout* ⟶

```
 1
 2
 3    (1)     General Information:
 4
 5          (i) APPLICANTS: Jeffrey M. Friedman, Yiying Zhang, Ricardo Proenca, Margherita
 6                Maffei, Jeffrey Halaas, Ketan Gajiwala, and Stephen K. Burley
 7
 8         (ii) TITLE OF INVENTION: MODULATORS OF BODY WEIGHT, CORRESPONDING NUCLEIC
 9                ACIDS AND PROTEINS, AND DIAGNOSTIC AND THERAPEUTIC USES THEREOF
10
11        (iii) NUMBER OF SEQUENCES: 99
12
13         (iv) CORRESPONDENCE ADDRESS:
14                (A) ADDRESSEE: Klauber & Jackson
15                (B) STREET: 411 Hackensack Avenue
16                (C) CITY: Hackensack
17                (D) STATE: New Jersey
18                (E) COUNTRY: USA
19                (F) ZIP: 07601
20
21         (v) COMPUTER READABLE FORM:
22                (A) MEDIUM TYPE: Floppy disk
23                (B) COMPUTER: IBM PC compatible
24                (C) OPERATING SYSTEM: PC-DOS/MS-DOS
25                (D) SOFTWARE: PatentIn Release #1.0, Version #1.25
26
27        (vi) CURRENT APPLICATION DATA:
28                (A) APPLICATION NUMBER: US 08/485,943
29                (B) FILING DATE: June 7, 1995
30                (C) CLASSIFICATION:
31
32       (vii) PRIOR APPLICATION DATA:
33                (A) APPLICATION NUMBER: 08/438,431
34                (B) FILING DATE: May 10, 1995
35                (C) CLASSIFICATION:
36
37       (vii) PRIOR APPLICATION DATA:
38                (A) APPLICATION NUMBER: 08/347,563
39                (B) FILING DATE: November 30, 1994
40                (C) CLASSIFICATION:
41
42       (vii) PRIOR APPLICATION DATA:
43                (A) APPLICATION NUMBER: 08/292,345
44                (B) FILING DATE: August 17, 1994
45                (C) CLASSIFICATION:
```

*INPUT SET: S9945.raw*

```
46
47        (viii) ATTORNEY/AGENT INFORMATION:
48               (A) NAME: Jackson Esq., David A.
49               (B) REGISTRATION NUMBER: 26,742
50               (C) REFERENCE/DOCKET NUMBER: 600-1-087 CIP2I
51
52        (ix) TELECOMMUNICATION INFORMATION:
53               (A) TELEPHONE: 201 487-5800
54               (B) TELEFAX: 201 343-1684
55               (C) TELEX: 133521
56
57
```

## ERRORED SEQUENCES FOLLOW:

```
429   (2) INFORMATION FOR SEQ ID NO:6:
430
431          (i) SEQUENCE CHARACTERISTICS:
432               (A) LENGTH: 167 amino acids
433               (B) TYPE: amino acid
434               (D) TOPOLOGY: linear
435
436          (ii) MOLECULE TYPE: protein
437               (A) DESCRIPTION: Human ob polypeptide lacking Gln at position 49
438
439          (vi) ORIGINAL SOURCE:
440               (A) ORGANISM: Human
441
442          (xi) SEQUENCE DESCRIPTION: SEQ ID NO:6:
443
444   Met His Trp Gly Thr Leu Cys Gly Phe Leu Trp Leu Trp Pro Tyr Leu
445    1               5                  10                  15
446
447   Phe Tyr Val Gln Ala Val Pro Ile Gln Lys Val Gln Asp Asp Thr Lys
448            20                  25                  30
449
450   Thr Leu Ile Lys Thr Ile Val Thr Arg Ile Asn Asp Ile Ser His Thr
451            35                  40                  45
452
453   Ser Val Ser Ser Lys Gln Lys Val Thr Gly Leu Asp Phe Ile Pro Gly
454            50                  55                  60
455
456   Leu His Pro Ile Leu Thr Leu Ser Lys Met Asp Gln Thr Leu Ala Val
457    65                  70                  75                  80
458
459   Tyr Gln Gln Ile Leu Thr Ser Met Pro Ser Arg Asn Val Ile Gln Ile
460                      85                  90                  95
461
462   Ser Asn Asp Leu Glu Asn Leu Arg Asp Leu Leu His Val Leu Ala Phe
463                 100                 105                 110
```

(handwritten annotation, right of lines 432–434): only 166 Showed up. IS one missing?

PAGE: 3

**RAW SEQUENCE LISTING**
PATENT APPLICATION   *US/08/485,943*

DATE: 04/17/96
TIME: 14:57:11

*INPUT SET: S9945.raw*

```
464
465      Ser Lys Ser Cys His Leu Pro Trp Ala Ser Gly Leu Glu Thr Leu Asp
466          115                 120             125
467
468      Ser Leu Gly Gly Val Leu Glu Ala Ser Gly Tyr Ser Thr Glu Val Val
469          130                 135             140
470
471      Ala Leu Ser Arg Leu Gln Gly Ser Leu Gln Asp Met Leu Trp Gln Leu
472      145             150                 155             160
473
474      Asp Leu Ser Pro Gly Cys
475                  165
476
477
```

```
478      (2) INFORMATION FOR SEQ ID NO:7:
479
480          (i) SEQUENCE CHARACTERISTICS:
-->  481              (A) LENGTH: 175 base pairs
482              (B) TYPE: nucleic acid
483              (C) STRANDEDNESS: double
484              (D) TOPOLOGY: linear
485
486          (ii) MOLECULE TYPE: DNA (genomic)
487              (A) DESCRIPTION: exon 2G7
488
489          (iii) HYPOTHETICAL: NO
490
491          (iv) ANTI-SENSE: NO
492
493          (xi) SEQUENCE DESCRIPTION: SEQ ID NO:7:
494
495      GTGCAAGAAG AAGAAGATCC CAGGGCAGGA AAATGTGCTG GAGACCCCTG TGTCGGGTCC          60
496
497      NGTGGNTTTG GTCCTATCTG TCTTATGTNC AAGCAGTGCC TATCCAGAAA GTCCAGGATG         120
498
-->  499      ACACCAAAAG CCTCATCAAG ACCATTGTCA NCAGGATCAC TGANATTTCA CACACG         175
500
501
```

*[handwritten annotations: "176 Showed up? Is there an extra? Review carefully & edit."]*
*[handwritten: "175" circled, "176?"]*

```
502      (2) INFORMATION FOR SEQ ID NO:8:
503
504          (i) SEQUENCE CHARACTERISTICS:
505              (A) LENGTH: 18 base pairs
506              (B) TYPE: nucleic acid
507              (C) STRANDEDNESS: single
508              (D) TOPOLOGY: linear
509
510          (ii) MOLECULE TYPE: DNA (primer)
-->  511              (A) PCR 5 primer for exon 2G7
512
513          (iii) HYPOTHETICAL: NO
514
```

*[handwritten: "Description: Insert subheading"]*

*INPUT SET: S9945.raw*

```
515        (iv) ANTI-SENSE: NO
516
517        (xi) SEQUENCE DESCRIPTION: SEQ ID NO:8:
518
519    CCAGGGCAGG AAAATGTG                                          18
520
521
```

```
522    (2) INFORMATION FOR SEQ ID NO:9:
523
524         (i) SEQUENCE CHARACTERISTICS:
525              (A) LENGTH: 22 base pairs
526              (B) TYPE: nucleic acid
527              (C) STRANDEDNESS: single
528              (D) TOPOLOGY: linear
529
530        (ii) MOLECULE TYPE: DNA (primer)
531              (A) PCR 3  primer for exon 2G7
532
533     (iii) HYPOTHETICAL: NO
534
535        (iv) ANTI-SENSE: YES
536
537
538        (xi) SEQUENCE DESCRIPTION: SEQ ID NO:9:
539
540    CATCCTGGAC TTTCTGGATA GG                                     22
541
542
543
```

*Description* (handwritten annotation pointing to lines 525-531)

```
623    (2) INFORMATION FOR SEQ ID NO:12:
624
625         (i) SEQUENCE CHARACTERISTICS:
626              (A) LENGTH: 45 amino acids
627              (B) TYPE: amino acid
628              (D) TOPOLOGY: linear
629
630        (ii) MOLECULE TYPE: protein
631
632        (xi) SEQUENCE DESCRIPTION: SEQ ID NO:12:
633
634    Met Gly Ser Ser His His His His His His Ser Ser Gly Leu Val Pro
635     1               5                   10                  15
636
637    Arg Gly Ser His Met Leu Glu Asp Pro Ala Ala Asn Lys Ala Arg Lys
638              20                  25                  30
639
640    Glu Ala Glu Leu Ala Ala Ala Thr Ala Glu Gln
641          35                  40
642
643
```

*Only 43 showed up.* (handwritten annotation pointing to line 626)

```
1231    (2) INFORMATION FOR SEQ ID NO:34:
```

*INPUT SET: S9945.raw*

```
1232
1233          (i) SEQUENCE CHARACTERISTICS:
1234              (A) LENGTH: 40 base pairs
1235              (B) TYPE: nucleic acid              Description
1236              (C) STRANDEDNESS: single
1237              (D) TOPOLOGY: linear
1238
1239         (ii) MOLECULE TYPE: DNA (primer)
-->  1240              (A) PCR 5  primer for amplifying human ob cDNA sequence
1241
1242        (iii) HYPOTHETICAL: NO
1243
1244         (iv) ANTI-SENSE: NO
1245
1246
1247         (xi) SEQUENCE DESCRIPTION: SEQ ID NO:34:
1248
1249    GTATCTCTCG AGAAAAGAGT GCCCATCCAA AAAGTCCAAG                    40
1250
1251
```

```
1252    (2) INFORMATION FOR SEQ ID NO:35:
1253
1254          (i) SEQUENCE CHARACTERISTICS:
1255              (A) LENGTH: 31 base pairs
1256              (B) TYPE: nucleic acid               descrip.
1257              (C) STRANDEDNESS: single
1258              (D) TOPOLOGY: linear
1259
1260         (ii) MOLECULE TYPE: DNA (primer)
-->  1261              (A) PCR 3  primer for amplifying human ob cDNA sequence
1262
1263        (iii) HYPOTHETICAL: NO
1264
1265         (iv) ANTI-SENSE: YES
1266
1267
1268         (xi) SEQUENCE DESCRIPTION: SEQ ID NO:35:
1269
1270    GCGCGAATTC TCAGCACCCA GGGCTGAGGT C                             31
1271
1272
```

```
1273    (2) INFORMATION FOR SEQ ID NO:36:
1274
1275          (i) SEQUENCE CHARACTERISTICS:
1276              (A) LENGTH: 40 base pairs
1277              (B) TYPE: nucleic acid               insert
1278              (C) STRANDEDNESS: single
1279              (D) TOPOLOGY: linear
1280
1281         (ii) MOLECULE TYPE: DNA (primer)
-->  1282              (A) PCR 5  primer for amplifying murine ob cDNA sequence
```

*INPUT SET: S9945.raw*

```
1283
1284        (iii) HYPOTHETICAL: NO
1285
1286        (iv) ANTI-SENSE: NO
1287
1288
1289        (xi) SEQUENCE DESCRIPTION: SEQ ID NO:36:
1290
1291   GTATCTCTCG AGAAAAGAGT GCCTATCCAG AAAGTCCAGG                    40
1292
1293
```

```
1294   (2) INFORMATION FOR SEQ ID NO:37:
1295
1296          (i) SEQUENCE CHARACTERISTICS:
1297              (A) LENGTH: 31 base pairs
1298              (B) TYPE: nucleic acid
1299              (C) STRANDEDNESS: single        insert
1300              (D) TOPOLOGY: linear
1301
1302         (ii) MOLECULE TYPE: DNA (primer)
-->  1303             (A) PCR 3  primer for amplifying murine ob cDNA sequence
1304
1305        (iii) HYPOTHETICAL: NO
1306
1307         (iv) ANTI-SENSE: YES
1308
1309
1310         (xi) SEQUENCE DESCRIPTION: SEQ ID NO:37:
1311
1312   GCGCGAATTC TCAGCATTCA GGGCTAACAT C                            31
1313
1314
```

```
2666   (2) INFORMATION FOR SEQ ID NO:95:
2667
2668              (i) SEQUENCE CHARACTERISTICS:                147 shown
-->  2669             (A) LENGTH  146 amino acids
2670              (B) TYPE: amino acid
2671              (D) TOPOLOGY: linear
2672
2673         (ii) MOLECULE TYPE: protein
2674              (A) DESCRIPTION: Recombinant murine met ob protein
2675
2676         (xi) SEQUENCE DESCRIPTION: SEQ ID NO:95:
2677
2678   Met Val Pro Ile Gln Lys Val Gln Asp Asp Thr Lys Thr Leu Ile Lys
2679    1           5                  10                  15
2680
2681   Thr Ile Val Thr Arg Ile Asn Asp Ile Ser His Thr Gln Ser Val Ser
2682              20                  25                  30
2683
2684   Ala Lys Gln Arg Val Thr Gly Leu Asp Phe Ile Pro Gly Leu His Pro
```

*INPUT SET: S9945.raw*

```
2685                35                          40                          45
2686
2687    Ile Leu Ser Leu Ser Lys Met Asp Gln Thr Leu Ala Val Tyr Gln Gln
2688         50                      55                      60
2689
2690    Val Leu Thr Ser Leu Pro Ser Gln Asn Val Leu Gln Ile Ala Asn Asp
2691     65                      70                      75                      80
2692
2693    Leu Glu Asn Leu Arg Asp Leu Leu His Leu Leu Ala Phe Ser Lys Ser
2694                    85                      90                      95
2695
2696    Cys Ser Leu Pro Gln Thr Ser Gly Leu Gln Lys Pro Glu Ser Leu Asp
2697                    100                     105                     110
2698
2699    Gly Val Leu Glu Ala Ser Leu Tyr Ser Thr Glu Val Val Ala Leu Ser
2700             115                     120                     125
2701
2702    Arg Leu Gln Gly Ser Leu Gln Asp Ile Leu Gln Gln Leu Asp Val Ser
2703         130                     135                     140
2704
2705    Pro Glu Cys
2706    145
2707
2708
```

# Notice of Availability

Applicant Aid for Biotechnology Computer Readable Form (CRF)
Sequence Listings Submissions

The Patent and Trademark Office (PTO) has developed a computer
program, called Checker, that will aid applicants in identifying
and correcting errors prior to making submissions for compliance
with the Requirements for Patent Applications Containing
Nucleotide Sequence and/or Amino Acid Sequence Disclosures
(sequence rules: 37 CFR 1.821 through 1.825).  (Final rules were
published in the *Federal Register* (55 FR 18230) on May 1, 1990,
and in the PTO *Official Gazette* (1114 Off.Gaz.PatOffice 29) on
May 15, 1990.)

Checker is a DOS-based software program that is intended to
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The most current version of the software will be available via
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1)    Dial-up access to the Patent and Trademark Office Bulletin
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      Phone number:  703-305-8950
      Cost: Free-of-charge
2)    Dial-up access through the Internet. FTP site: ftp.uspto.gov
      Login as "anonymous".  Software is in directory /pub/checker
      Cost: Free-of-charge
3)    For diskette copies, telephone requests to 703-306-2600.
      Cost: $25.00

*For Further Information Contact:* Meredith Beckhardt at 703-308-4212.

# NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☐ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to these regulations, published at 1114 OG 29, May 15, 1990 and at 55 FR 18230, May 1, 1990.

☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☒ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☐ 7. Other: _____

## Applicant Must Provide:

☒ An initial or <u>substitute</u> computer readable form (CRF) copy of the "Sequence Listing".

☒ An initial or <u>substitute</u> paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216
For CRF Submission Help, call (703) 308-4212
For PatentIn software help, call (703) 308-6856

## PLEASE RETURN A COPY OF THIS NOTICE WITH YOUR RESPONSE